REMARKS/ARGUMENTS

Applicants wish to thank Examiner Balasubramanian for the thorough examination of the present application. Upon entry of the present amendment, claims 1, 6-12, 17 and 19-21 will be pending. Claims 2-5, 13-16 and 18 remain canceled without prejudice or disclaimer. Applicants reserve the right to pursue the canceled claims in the present application or in a continuation application. Claims 1, 6-10 and 20 have been amended. Support for the amendment to the definition of "C_{3-8}heterocycloalkyl-C_{0-4}alkyl" of claim 1 is found on page 5, lines 1-4 of the specification as originally filed. Support for the amendment to the definitions of aryl substituents of claim 1 is found in originally filed claim 1. Support for the amendments to claims 6-10 is found in originally filed claims 1 and 6-10. No new matter has been introduced. Reconsideration of the rejected claims is respectfully requested.

I. Rejection of Claims 1, 6-12, 17 and 19-21 under 35 U.S.C. §112, Second Paragraph.

Claims 1, 6-12 , 17 and 19-21 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Without acquiescing to the merits and in the interest of expediting prosecution, Applicants have amended claims 1, 6-10 and 20 to obviate the rejections. In view of the amendments, Applicants respectfully request that the rejections under 35 U.S.C. §112, second paragraph, be withdrawn.

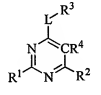
II. Rejections under 35 U.S.C. § 102(b)

A. Rejection of Claims 1, 6-8, 11 and 17 Over Kiyama

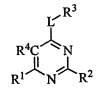
Claims 1, 6-8, 11 and 17 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Kiyam et al. (WO 2003/016275; U.S. Patent Application Publication No. 2004/0229909, hereinafter "Kiyama"). To expedite prosecution, Applicants have amended claim 1, 6-10 and 20. In view of the amendments, Applicants respectfully traverse the rejection.

As set forth in MPEP §2131, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.

Applicants submit that Kiyama does not disclose the compounds of Formula I recited in amended claim 1, thus, Kiyama does not anticipate the claimed invention. Amended claim 1 recites a compound of Formula I, which has two possible core structures, i.e., structure **I-A** (X^1= -N= and X^2 = -CR^4=) and structure **I-B** (X^1 = -CR^4= and X^2 = -N=):



I-A



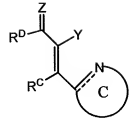
I-B

wherein $\mathbf{R^2}$ is hydrogen, amino, C_{1-4}alkoxy and halo-substituted C_{1-4}alkoxy; **L** is a bond, -O- and -NR^5-, wherein R^5 is hydrogen or C_{1-4}alkyl; $\mathbf{R^3}$ is (i) C_{3-8}heterocycloalkyl-C_{0-4}alkyl selected from the group consisting of morpholino, morpholino-methyl, morpholino-ethyl, pyrrolidinyl, piperazinyl, piperidinyl, 4-oxo-piperidin-1-yl and 1,4-dioxa-8-aza-spiro[4,5]dec-8-yl, (ii) C_{5-10}heteroaryl-C_{0-4}alkyl, wherein the heteroaryl is optionally substituted, (iii) substituted C_{6-10}aryl-C_{0-4}alkyl and (iv) $-X^3NR^8R^8$, wherein X^3 is a bond or alkylene and R^8 is hydroxyalkyl or alkenyl; $\mathbf{R^4}$ is –H or C_{1-4}alkyl.

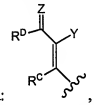
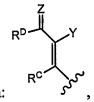
In structure **I-A**, R^1 is selected from the group consisting of -$X^3NR^6R^7$, wherein X^3 is-C_{1-4}alkylene, R^6 is hydrogen and R^7 is selected from the group consisting of C_{6-10}aryl and C_{5-6}heteroaryl; wherein the aryl or heteroaryl is optionally substituted with 1 to 3 radicals independently selected from the group consisting of halo, amino, C_{1-4}alkyl, halo-substituted C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted C_{1-4}alkoxy.

In structure **I-B**, R^1 is -$X^3NR^6R^7$, wherein X^3 is a bond or C_{1-4}alkylene, R^6 is hydrogen or C_{1-4}alkyl and R^7 is selected from the group consisting of C_{6-10}aryl and C_{5-6}heteroaryl; wherein the heteroaryl is optionally substituted with 1 to 3 radicals independently selected from the group consisting of halo, amino, C_{1-4}alkyl, halo-substituted C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted C_{1-4}alkoxy, and R^2 is hydrogen, amino, alkoxy, haloalkoxy, wherein the aryl moiety of R^1 ***is substituted*** with 1 to 3 radicals independently selected from the group consisting of amino, halo-substituted C_{1-4}alkyl, and halo-substituted C_{1-4}alkoxy.

In contrast, Kiyama discloses a generic structure of formula I:



I

wherein R^C and R^D taken together with the neighboring carbon atoms form a ring which may be a condensed ring, Y is hydroxyl, mercapto or amino; and Z is O, S or NH, wherein C ring is N-containing aromatic heterocycle. Therefore, formula I of Kiyama discloses an aromatic heterocycle (C ring) having a substituent represented by the formula:  , wherein ***Z is an oxo (=O), thioxo (=S) or imino (=NH)***. In other words, Kiyama discloses that the substituent has the formula:  , wherein the ***ring carbon*** is substituted by ***=O, =S or =NH group***.

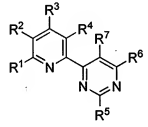
The substituents in structures **I-A** and **I-B** of the compounds of the present invention are R^1, R^2, -L-R^3 and R^4. As recited in amended claim 1, R^2 is hydrogen, amino, C_{1-4}alkoxy or halo-substituted C_{1-4}alkoxy. L is a bond, -O- and -NR^5-, wherein R^5 is hydrogen or C_{1-4}alkyl. R^3 is optionally substituted (a) C_{3-8}heterocycloalkyl-C_{0-4}alkyl selected from the group consisting of morpholino, morpholino-methyl, morpholino-ethyl, pyrrolidinyl, piperazinyl, piperidinyl, 4-oxo-piperidin-1-yl and 1,4-dioxa-8-aza-spiro[4,5]dec-8-yl, (b) C_{5-10}heteroaryl-C_{0-4}alkyl, (c) C_{6-10}aryl-C_{0-4}alkyl and (d)-$X^3NR^8R^8$; R^4 is –H or C_{1-4}alkyl. R^1 in structure **I-A** is -$X^3NR^6R^7$ (arylamino or heteroarylamino, X^3 = bond; or arylaminoalkyl or heteroarylaminoalkyl, X^3 = alkylene). R^1 in structure **I-B** is –$X^3NR^6R^7$ (arylamino or heteroarylamino, X^3 = bond; or arylaminoalkyl or heteroarylaminoalkyl, X^3 =alkylene). None of the substituents R^1, R^2, -L-R^3 and R^4 in structures **I-A** and **I-B** recite a heterocycle substituent, wherein the ***ring carbon*** is substituted by ***=O, =S or =NH group*** as required in Kiyama Hence,

Kiyama fails to teach the compounds of formula I recited in amended claim 1, thus, amended claim 1 is not anticipated by Kiyama. Since claims 6-8, 11 and 17 are dependent from claim 1 and therefore incorporate all the limitations of claim 1, claims 6-8, 11 and 17 are not anticipated by Kiyama. Accordingly, Applicants respectfully request that this anticipation rejection of claims 1, 6-8 and 17 over Kiyama be withdrawn.

B. Rejection of Claims 1, 6-8, 11 and 17 Over Hoffmann

Claims 1, 6-8, 11 and 17 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Hoffmann et al. (DE 4031798, hereinafter "Hoffmann"). To expedite prosecution, Applicants have amended claims 1, 6-10 and 20. In view of the amendments, Applicants respectfully traverse the rejection.

Applicants submit that Hoffmann does not disclose the compounds of amended claim 1, thus, it does not anticipate the claimed invention. Hoffmann discloses compounds having formula (I):



(I)

wherein:

$\mathbf{R^1}$ and $\mathbf{R^3}$ are each independently –H, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_4)$alkoxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkylthio-$(C_1\text{-}C_4)$alkyl, $(C_2\text{-}C_6)$alkinyl,$C_3\text{-}C_7)$cycloalkyl, $(C_3\text{-}C_7)$cycloalkyl-$(C_1\text{-}C_4)$alkyl, phenyl-$(C_1\text{-}C_4)$alkyl, phenyl, phenoxy-$(C_1\text{-}C_4)$alkyl, phenylmercapto-$(C_1\text{-}C_4)$alkyl, wherein the phenyl moiety of the last four groups is optionally substituted with from one to three substituents selected from halogen, -CN, $-NO_2$, $(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy, $(C_1\text{-}C_4)$alkylthio, $(C_1\text{-}C_4)$haloalkyl or $(C_1\text{-}C_4)$haloalkoxy, or $\mathbf{R^1}$ and $\mathbf{R^3}$ can be halogen, $(C_1\text{-}C_4)$haloalkyl, $(C_1\text{-}C_6)$alkoxy;

$\mathbf{R^2}$ and $\mathbf{R^4}$ are each independently –H, $(C_1\text{-}C_6)$alkyl, halogen, $(C_1\text{-}C_4)$haloalkyl, $(C_1\text{-}C_6)$alkoxy;

$\mathbf{R^5}$ is -H, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_1\text{-}C_4)$alkoxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkylthio-$(C_1\text{-}C_4)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkinyl, $(C_3\text{-}C_7)$acycloalkyl-$(C_1\text{-}C_4)$alkyl, phenyl, phenyl-$(C_1\text{-}$

C_4)alkyl, benzyloxy-(C_1-C_4)alkyl, where the phenyl moiety of the last three groups is optionally substituted with from one to three substituents selected from halogen, -NO_2, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, (C_1-C_4)alkylthio, (C_1-C_4)haloalkyl or (C_1-C_4)haloalkoxy, or $\mathbf{R^5}$ can be (C_2-C_6)alkinyloxy-(C_1-C_4)alkyl, (C_2-C_6)alkenyloxy-(C_1-C_4)alkyl;

$\mathbf{R^6}$ is -H, (C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl-(C_1-C_4)alkyl, wherein the cycloalkyl moiety of the last two groups is optionally substituted with from one to three (C_1-C_4)alkyl, or R^6 can be (C_1-C_4)haloalkyl, (C_1-C_{12})alkoxy, (C_1-C_4)alkylthio, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkylthio-(C_1-C_4)alkyl, halogen, (C_2-C_6)alkenyl, (C_2-C_6)alkinyl, phenyl, phenyl-(C_1-C_4)alkyl, phenyl-(C_1-C_4)alkoxy or phenyl-(C_1-C_4)alkylthio, wherein the phenyl moiety of the last four groups is optionally substituted with from one to three substituents selected from halogen, -CN, -NO_2, (C_1-C_4)haloalkyl, (C_1-C_4)alkoxy, (C_1-C_4)alkyl or (C_1-C_4)haloalkoxy, or $\mathbf{R^6}$ can be (C_2-C_6)alkinyloxy-(C_1-C_4)alkoxy, (C_2-C_6)alkenyl-(C_1-C_4)alkoxy, (C_2-C_6)alkinyloxy-(C_1-C_4)alkylthio, (C_2-C_6)alkenyl-(C_1-C_4)alkylthio, (C_1-C_4)alkylsulfonyl, NR^8R^9, wherein:

$\mathbf{R^8}$ and $\mathbf{R^9}$ are each independently –H, (C_1-C_6)alkyl, (C_3-C_6)alkenyl, (C_3C_6)alkinyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl-(C_1-C_4)alkyl, formyl, phenyl, phenyl-(C_1-C_4)alkyl, where the phenyl moiety of the last two groups is optionally substituted with from one to three substituents selected from halogen, -CN, -NO_2, (C_1-C_4)alkyl, (C_1-C_4)alkoxy; or $\mathbf{R^8}$ and $\mathbf{R^9}$ together with the N to which they are attached form an unsubstd. or substituted up to four 5-7 membered saturated or unsaturated heterocycle with 1-3 the same or different hetero atoms;

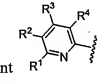
$\mathbf{R^7}$ is –H, (C_1-C_4)alkyl, halogen.

Applicants assert that Hoffmann does not disclose compounds having structure **I-A** in amended claim 1. The substituent R^5 in formula (I) of Hoffmann corresponds to the substituent R^1 in structure **I-A** of the present invention. As recited in amended claim 1, R^1 in structure **I-A** is -$X^3NR^6R^7$ (arylamino or heteroarylamino, X^3 = bond; or arylaminoalkyl or heteroarylaminoalkyl, X^3 = alkylene). As discussed above, R^5 in formula (I) of Hoffmann is -H, (C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkylthio-(C_1-C_4)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkinyl, (C_3-C_7)acycloalkyl-(C_1-C_4)alkyl, phenyl, phenyl-(C_1-C_4)alkyl, benzyloxy-(C_1-C_4)alkyl, where the phenyl moiety of the last three groups is optionally substituted with from one to three substituents selected from halogen, -NO_2, (C_1-C_4)alkyl, (C_1-

C_4)alkoxy, (C_1-C_4)alkylthio, (C_1-C_4)haloalkyl or (C_1-C_4)haloalkoxy, or R^5 can be (C_2-C_6)alkinyloxy-(C_1-C_4)alkyl, (C_2-C_6)alkenyloxy-(C_1-C_4)alkyl. None of the R^5 substituents in formula (I) of Hoffmann can be $-X^3NR^6R^7$ as recited for substituent R^1 in structure **I-A** of amended claim 1. Therefore, Hoffmann fails to teach the compounds having structure **I-A** as recited in amended claim 1.

Applicants further assert that Hoffmann does not teach compounds having

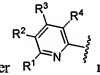
structure **I-B** as recited in amended claim 1. The substituents and R^6 in formula (I) of Hoffmann correspond to the substituents R^1 and $-L-R^3$ in structure **I-B** of the present invention. As recited in amended claim 1, R^1 is $-X^3NR^6R^7$ (arylamino or heteroarylamino, X^3 = bond; or arylaminoalkyl or heteroarylaminoalkyl, X^3 = alkylene), wherein the heteroaryl is optionally substituted with 1 to 3 radicals independently selected from the group consisting of halo, amino, C_{1-4}alkyl, halo-substituted C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted C_{1-4}alkoxy, wherein ***the aryl moiety of R^1 is substituted*** with 1 to 3 radicals independently selected from the group consisting of ***amino, halo-substituted C_{1-4}alkyl and halo-substituted C_{1-4}alkoxy***.



In contrast, the substituent in Formula (I) of Hoffmann represents a substituted or unsubstituted 2-pyridyl directly attached to the pyrimidine ring. Hoffmann does

not disclose that the substituent can be heteroarylamino, heteroarylaminoalkyl, arylamino or arylaminoalkyl as recited for R^1 in structure **I-B**. As discussed above, R^6 in formula (I) of Hoffmann can be -H, (C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl-(C_1-C_4)alkyl, wherein the cycloalkyl moiety of the last two groups is optionally substituted with from one to three (C_1-C_4)alkyl, or R^6 can be (C_1-C_4)haloalkyl, (C_1-C_{12})alkoxy, (C_1-C_4)alkylthio, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkylthio-(C_1-C_4)alkyl, halogen, (C_2-C_6)alkenyl, (C_2-C_6)alkinyl,

phenyl, phenyl-(C_1-C_4)alkyl, phenyl-(C_1-C_4)alkoxy or phenyl-(C_1-C_4)alkylthio, wherein the phenyl moiety of the last four groups is optionally substituted with from one to three substituents selected from halogen, -CN, -NO_2, (C_1-C_4)haloalkyl, (C_1-C_4)alkoxy, (C_1-C_4)alkyl or (C_1-C_4)haloalkoxy, or R^6 can be (C_2-C_6)alkinyloxy-(C_1-C_4)alkoxy, (C_2-C_6)alkenyl-(C_1-C_4)alkoxy, (C_2-C_6)alkinyloxy-(C_1-C_4)alkylthio, (C_2-C_6)alkenyl-(C_1-C_4)alkylthio, (C_1-C_4)alkylsulfonyl, NR^8R^9, wherein R^8 and R^9 are each independently –H, (C_1-C_6)alkyl, (C_3-C_6)alkenyl, (C_3-C_6)alkinyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl-(C_1-C_4)alkyl, formyl, phenyl, phenyl-(C_1-C_4)alkyl, where the phenyl moiety of the last two groups is optionally substituted with from one to three substituents selected from halogen, -CN, -NO_2, (C_1-C_4)alkyl, (C_1-C_4)alkoxy; or R^8 and R^9 together with the N to which they are attached form an unsubstd. or substituted up to four 5-7 membered saturated or unsaturated heterocycle with 1-3 the same or different hetero atoms. However, none of the Markush members of R^6 in Hoffmann can be heteroarylamino, heteroarylaminoalkyl, arylamino or arylaminoalkyl, wherein ***the aryl moiety is substituted*** with 1 to 3 radicals independently selected from the group consisting of ***amino, halo-substituted C_1-$_4$alkyl and halo-substituted C_1-$_4$alkoxy***, the substituents as recited for the aryl moiety of R^1 in



structure **I-B**. Therefore, neither nor R^6 in Formula I of Hoffmann discloses (or allows for) the R^1 substituent of structure **I-B**. Hence, Hoffman fails to teach the compounds of structure **I-B** as recited in claim 1. Thus, Hoffmann discloses neither the compounds of structure **I-A**, nor the compounds of structure **I-B** as recited in amended claim 1. As a result, amended claim 1 is not anticipated by Hoffmann. Since claims 6-8, 11 and 17 are dependent from claim 1 and therefore incorporate all the limitations of claim 1, claims 6-8, 11 and 17 are not anticipated by Hoffmann. Accordingly, Applicants respectfully request that this anticipation rejection of claims 1, 6-8 and 17 over Hoffmann be withdrawn.

C. Rejection of Claims 1, 6-8, 11 and 17 Over Yamanaka

Claims 1, 6-8, 11 and 17 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Yamanaka et al. (*Chem. Pharm. Bull.* 28(5), 1526-1533, 1980, hereinafter

"Yamanaka"). To expedite prosecution, Applicants have amended claim 1, 6-10 and 20. In view of the amendments, Applicants respectfully traverse the rejection.

Applicants submit that Yamanaka does not teach the compounds of the claimed invention. Yamanaka discloses the synthesis of a number of pyrimidine derivatives including the N-oxide derivatives. Specifically, Yamanaka discloses the following compounds (I, III, Iva, IVb, VII, VIII, XIII, XIV, XVI, XVII, XVIII, XIX, XX, XXIVa, XXIVb, XXIIIa, XXIIIb and XXV) as collectively represented by formula (IY):

IY

I: Rx = CH_3, Ry = CH_3, Rz = H

IIII: Rx =Ry = -CH=CHPh, Rz = H

IVa: Rx = CH_3, Ry = Ph, Rz = H

IVb: Rx = OEt, Ry = CH_3, Rz = H

VII: Rx = Ph, Ry = -CH=CHPh, Rz = H

VIII: Rx = Ph, Ry = $-CH_2CH_2Ph$, Rz = H

XIII: Rx = Ph, Ry = -CH=CHPh, Rz = CH_3

XIV: Rx = Ph, Ry = I, Rz = CH_3

XVI: Rx =Ry = -CH=CHPh, Rz = CH_3

XVII: Rx =Ry = Rz -CH=CHPh

XVIII: Rx =Ry = $-CH_2CH_2Ph$, Rz = CH_3

XIX: Rx =Ry = I, Rz = CH_3

XX: Rx =Ry = -CCPh, Rz = CH_3

XXIVa,b: Rx = Ph or OEt, Ry = piperidinyl-ethyl, Rz = H

XXV: Rx = Ph, Ry = piperidinyl-propen-2yl, Rz = H

XXIIIa,b: Rx = Ph or OEt, Ry = 1,3-bispiperidinyl-2-propyl, Rz = H

Applicants submit that Yamanaka does not teach compounds having structure **I-A**. The substituent Rz in formula IY of Yamanaka corresponds to the substituent R^1 in structure **I-A** of amended claim 1. Rz in formula I of Yamanaka is H or CH_3. As recited in amended claim 1, R^1 in structure **I-A** is $-X^3NR^6R^7$ (arylamino or heteroarylamino, X^3 = bond; or arylaminoalkyl or heteroarylaminoalkyl, X^3 = alkylene). Amended claim 1 does not recite that R^1 in structure **I-A** is hydrogen or CH_3 as disclosed in Yamanaka. Therefore, Yamanaka fails to teach the compounds of structure **I-A** as recited in amended claim 1.

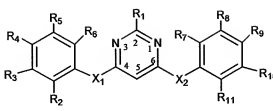
Applicants further submit that Yamanaka does not teach the compounds having structure **I-B** as recited in amended claim 1. The susbtituents Rx and Ry correspond to the

substituents R^1 and $-L-R^3$ in structure **I-B** of the present invention. Applicants submit that Yamanaka does not teach the R^1 substituent in structure **I-B**. As shown above, Rx is CH_3, -OEt, Ph, -CH=CHPh, $-CH_2CH_2Ph$, -CCPh or I; and Ry is CH_3, Ph, -CH=CHPh, $-CH_2CH_2Ph$, -CCPh, I, piperidinyl-ethyl, 1,3-bispiperidinyl-2-propyl or piperidinyl-propen-2yl. As recited in amended claim 1, R^1 is $-X^3NR^6R^7$ (arylamino or heteroarylamino, X^3 = bond; or arylaminoalkyl or heteroarylaminoalkyl, X^3 = alkylene), wherein the heteroaryl is optionally substituted with 1 to 3 radicals independently selected from the group consisting of halo, amino, C_{1-4}alkyl, halo-substituted C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted C_{1-4}alkoxy, wherein ***the aryl moiety of R^1 is substituted*** with 1 to 3 radicals independently selected from the group consisting of ***amino, halo-substituted C_{1-4}alkyl and halo-substituted C_{1-4}alkoxy.*** Thus, R^1 in structure **I-B** does not recite CH_3, -OEt, Ph, -CH=CHPh, $-CH_2CH_2Ph$, -CCPh, I, piperidinyl-ethyl, 1,3-bispiperidinyl-2-propyl or piperidinyl-propen-2yl substituents as disclosed for Rx and Ry in the compounds of Yamanaka. Hence, Yamanaka fails to teach the compounds of structure **I-B** as recited in amended claim 1. Consequently, Yamanaka discloses neither the compounds of structure **I-A**, nor the compounds of structure **I-B** as recited in amended claim 1. As such, Yamanaka does not teach the compounds of Formula I as recited in amended claim 1, thus, claim 1 is not anticipated by Yamanaka. Since claims 6-8 and 11 are dependent from claim 1 and therefore incorporate all the limitations of claim 1, claims 6-8 and 11 are not anticipated by Yamanaka. Accordingly, Applicants respectfully request that this anticipation rejection of claims 1, 6-8 and 11 over Yamanaka be withdrawn.

D. Rejection of Claims 1, 6, 9, 10 and 17 Over Cuccia

Claims 1, 6, 9, 10 and 17 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Cuccia *et al.* (U.S. Patent No. 6,281,219, hereinafter "Cuccia"). To expedite prosecution, Applicants have amended claim 1, 6-10 and 20. In view of the amendments, Applicants respectfully traverse the rejection.

Applicants submit that Cuccia does not teach each and every element of the claimed invention and, thus, Cuccia does not anticipate the claimed invention. Cuccia teaches pyrimidine derivatives having the formula:



wherein: $\mathbf{R_1}$ is hydrogen, $(C_{1\text{-}6})$alkylthio, halo$(C_{1\text{-}6})$alkylthio, $(C_{1\text{-}6})$alkylsulphinyl, halo$(C_{1\text{-}6})$alkylsulfinyl, $(C_{1\text{-}6})$alkylsulphonyl, halo$(C_{1\text{-}6})$alkylsulphonyl or $NR_{12}R_{13}$; R_{12} and R_{13} are each independently hydrogen, $(C_{1\text{-}6})$alkyl, or halo$(C_{1\text{-}6})$alkyl; $\mathbf{X_1}$ and $\mathbf{X_2}$ are independently selected from the group consisting of NR_{14}, NR_{15}, O, CH_2, $CR_{18}R_{19}$, CO and C=NOR_{20}; R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{11} are each independently selected from hydrogen, halogen, cyano, nitro, $C_{1\text{-}6}$alkyl, halo$(C_{1\text{-}6})$alkyl, $(C_{1\text{-}6})$alkoxy, halo$(C_{1\text{-}6})$alkoxy, $(C_{1\text{-}6})$alkoxy$(C_{1\text{-}6})$alkyl, halo$(C_{1\text{-}6})$alkoxy$(C_{1\text{-}6})$alkyl, $(C_{1\text{-}6})$alkylthio, halo$(C_{1\text{-}6})$alkylthio, $(C_{1\text{-}6})$alkylsulphinyl, halo$(C_{1\text{-}6})$alkylsuphinyl, $(C_{1\text{-}6})$alkylsulphonyl, halo$(C_{1\text{-}6})$alkylsulphonyl, amino, $(C_{1\text{-}6})$alkylamino, di$(C_{1\text{-}6})$alkylamino, halo$(C_{1\text{-}6})$alkylamino, $(C_{1\text{-}6})$alkylhaloalkyl$(C_{1\text{-}6})$amino, dihalo$(C_{1\text{-}6})$alkylamino, $(C_{1\text{-}6})$alkoxy-carbonyl, halo$(C_{1\text{-}6})$alkoxycarbonyl, $C_{2\text{-}6}$alkenyl, halo$(C_{2\text{-}6})$alkenyl, $(C_{2\text{-}6})$alkynyl, halo$(C_{2\text{-}6})$alkynyl; and R_{10} is halogen, halo$(C_{1\text{-}6})$alkyl, halo$(C_{2\text{-}6})$alkenyl or halo$(C_{2\text{-}6})$alkynyl. The substituents at the 4 and 6 positions are represented by **X_1-aryl** and **X_2-aryl**, where aryl represents phenyl group having R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and R_{11} substituents.

Applicants assert that Cuccia does not teach a compound having core structure **I-A**. The substituent R^1 on the pyrimidine ring in Cuccia occupies the position that corresponds to R^1 in **I-A**. Cuccia discloses that R^1 is hydrogen, $(C_{1\text{-}6})$alkylthio, halo$(C_{1\text{-}6})$alkylthio, $(C_{1\text{-}6})$alkylsulphinyl, halo$(C_{1\text{-}6})$alkylsulfinyl, $(C_{1\text{-}6})$alkylsulphonyl, halo$(C_{1\text{-}6})$alkylsulphonyl or $NR_{12}R_{13}$; R_{12} and R_{13} are each independently hydrogen, $(C_{1\text{-}6})$alkyl, or halo$(C_{1\text{-}6})$alkyl. Clearly, Cuccia does not teach that the substituent R^1 can be $-X^3NR^6R^7$ (arylamino or heteroarylamino, X^3 = bond; or arylaminoalkyl or heteroarylaminoalkyl, X^3 = alkylene) as recited for R^1 in structure **I-A**. Therefore, a compound having structure **I-A** is not anticipated by Cuccia.

Applicants further assert that Cuccia does not teach a compound having core structure **I-B**. Substituents X_1-aryl and X_2-aryl on the pyrimidine ring in Cuccia occupy the positions that correspond to R^1 and L-R^3 in structure **I-B**. Cuccia teaches X_1-aryl and X_2-aryl

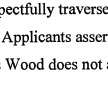
having substituents R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and R_{11}, but ***does not*** teach that substituents R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and R_{11} are hydroxy-$C_{1\text{-}6}$alkyl, phenyl, $C_{3\text{-}8}$heterocycloalkyl, $-X^3C(O)NR^8R^8$, $-X^3C(O)NR^8R^9$, $-X^3C(O)R^9$, $-X^3S(O)NR^8R^8$, $-X^3NR^8R^9$, $-X^3S(O)_2NR^8R^8$, $-X^3S(O)_2R^9$, $-X^3SNR^8R^8$, $-X^3ONR^8R^8$, $-X^3C(O)R^8$, $-X^3NR^8C(O)R^8$, $-X^3NR^8S(O)_2R^8$, $-X^3S(O)_2NR^8R^9$, $X^3NR^8S(O)_2R^9$, $-X^3NR^8C(O)R^9$, $-X^3NR^8C(O)NR^8R^9$, $-X^3NR^8C(O)NR^8R^8$, $=NOR^8$, $-X^3NR^8OR^8$, $-X^3NR^8(CH_2)_{1\text{-}4}NR^8R^8$, $-X^3C(O)NR^8(CH_2)_{1\text{-}4}NR^8R^8$, $-X^3C(O)NR^8(CH_2)_{1\text{-}4}R^9$, $-X^3C(O)NR^8(CH_2)_{1\text{-}4}OR^9$, $-X^3O(CH_2)_{1\text{-}4}NR^8R^8$, $-X^3C(O)NR^8(CH_2)_{1\text{-}4}OR^8$and $X^3NR^8(CH_2)_{1\text{-}4}R^9$, the substituents that are recited for the ***aryl portion*** of ***the R^3 group*** in amended claim 1. Therefore, a compound of structure **I-B** is not anticipated by Cuccia.

Since core structures **I-A** or **I-B** of the compounds of Formula I are not disclosed by Cuccia, claim 1 is not anticipated by Cuccia. Since claims 6, 9, 10 and 17 are dependent from claim 1 and, therefore, incorporate all the limitations of claim 1, claims 6, 9, 10 and 17 are not anticipated by Cuccia. Accordingly, Applicants respectfully request that the rejection of claims 1, 6, 9 10 and 17 over Cuccia under 35 U.S.C. §102(b) be withdrawn.

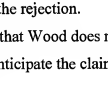
E. Rejection of Claims 1, 6, 9, 10 and 17 Over Wood

Claims 1, 6, 9, 10 and 17 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Wood *et al.* (U.S. Patent No. 6,306,866, hereinafter "Wood"). To expedite prosecution, Applicants have amended claim 1, 6-10 and 20. In view of the amendments, Applicants respectfully traverse the rejection.

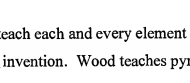
Applicants assert that Wood does not teach each and every element of the invention, thus Wood does not anticipate the claimed invention. Wood teaches pyrimidine derivatives having the formulae:



IA



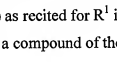
IB



IB1 ,

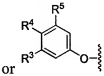
wherein: A represents a phenyl group being substituted by one or more of the same or different substituents selected from halogen atoms, alkyl, alkoxy, cyano, nitro, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, alkylsuphinyl, alkylsulphonyl and SF_5 groups. B represents a phenyl group being substituted by one or more of the same or different substituents selected from halogen atoms, alkyl, alkoxy, cyano, nitro, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, alkylsulphinyl, alkylsulphonyl and SF_5 groups. R^1 and R^2 each independently represents a hydrogen or halogen atom or an alkyl, alkenyl, alkinyl, alkoxy, alkoxyalkyl, alkoxyalkoxy group, alkylthio, alkylsulphinyl or alkylsulphonyl group, an amino, alkylamino or dialkylamino group or a cyano, nitro, haloalkyl, haloalkoxy, haloalkylthio or SF_5 group,

Applicants assert that a compound having core structure **I-A** is not anticipated by a compound of formula **IA** in Wood. The substituent R^1 on the pyrimidine ring in **IA** of Wood corresponds to R^1 in structure **I-A** of amended claim 1. The R^1 in formula **IA** of Wood is a hydrogen or halogen atom or an alkyl, alkenyl, alkinyl, alkoxy, alkoxyalkyl, alkoxyalkoxy group, alkylthio, alkylsulphinyl or alkylsulphonyl group, an amino, alkylamino or dialkylamino group or a cyano, nitro, haloalkyl, haloalkoxy, haloalkylthio or SF_5 group. Clearly, formula **IA** does not teach (or allow for) the substituent R^1 to be $-X^3NR^6R^7$ (arylamino or heteroarylamino, X^3 = bond; or arylaminoalkyl or heteroarylaminoalkyl, X^3 = alkylene) as recited for R^1 in structure **I-A**. Therefore, a compound of structure **I-A** is not anticipated by a compound of the formula **IA** in Wood.

Applicants further assert that the core structure **I-A** is not anticipated by a compound of formula **IB** or **IB1** of Wood. The substituent A-O- or  on the pyrimidine ring in structure **IB** or **IB1** of Wood occupies the positions that correspond to R^1 in structure **I-A**. The substituents A-O- and  in formulas **IB** and **IB1** of Wood are substituted or unsubstituted phenoxy. Formula **IB** or **IB1** in Wood does not teach (or allow for)

substituent A-O- or  to be -$X^3NR^6R^7$ (arylamino or heteroarylamino, X^3 = bond; or arylaminoalkyl or heteroarylaminoalkyl, X^3 = alkylene) as recited for R^1 in structure **I-A**. Thus, compounds having structure **I-A** are not anticipated by a compound of the formula **IB** or **IB1** in Wood.

Applicants submit that the compounds of core structure **I-B** are not anticipated by a compound of formula **IA** in Wood. Substituents A-O and B on the pyrimidine ring in formula **IA** occupy the positions that correspond to R^1 and L-R^3 in structure **I-B**. Wood teaches A-O and B to be substituted phenoxy or phenyl groups, wherein the substituents on the phenyl ring are halogen atoms, alkyl, alkoxy, cyano, nitro, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, alkylsuphinyl, alkylsulphonyl and SF_5 groups, but **does not** teach the substituent -$X^3NR^6R^7$ (arylamino or heteroarylamino, X^3 = bond; or arylaminoalkyl or heteroarylaminoalkyl, X^3 = alkylene) as recited for R^1 in structure **I-B**. Therefore, compounds of the structure **I-B** are not anticipated by a compound of formula **I-A** in Wood.

Applicants further submit that the core structure **I-B** is not anticipated by a compound of formula **IB or IB1** in Wood. The substituent A-O- or  on the pyrimidine ring in structure **IB** or **IB1** of Wood occupies the position that corresponds to R^2 in structure **I-B**. The substituents A-O- and  in formulas **IB** and **IB1** of Wood are substituted or unsubstituted phenoxy. Formula **IB** or **IB1** in Wood does not teach (or allow for) substituent A-O- or  to be hydrogen, amino, alkoxy or haloalkoxy as recited for R^2

in structure **I-B**. Thus, compounds of structure **I-B** are not anticipated by a compound of the formula **IB** or **IB1** in Wood.

Again, since core structures **I-A** or **I-B** of the compounds of Formula I are not disclosed by Wood, amended claim 1 is not anticipated by Wood. As claims 6, 9, 10 and 17 are dependent from claim 1 and, therefore, incorporate all the limitations of claim 1, claims 6, 9, 10 and 17 are not anticipated by Wood. Accordingly, Applicants respectfully request that the rejection of claims 1, 6, 9 10 and 17 over Wood under 35 U.S.C. §102(b) be withdrawn.

III. Claim Rejections 35 U.S.C. § 103(a)

A. Rejection of claims 1, 6-11 and 17 over Kiyama

Claims 1, 6-11 and 17 have been rejected as allegedly being obvious over Kiyama. To the extent that the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

As discussed in section IIA above, amended claims 1, 6-8, 11 and 17 are novel over the compounds of Kiyama. The compounds of the present invention are ***structurally different*** from those disclosed in Kiyama and none of the compounds of Kiyama are embraced in the presently claimed compounds of Formula I of amended claim 1. In addition, there are no teachings or suggestions in Kiyama to modify the compounds of Kiyama to arrive at the compounds of the presently claimed invention. Accordingly, Applicants respectfully request the rejection of claims 1, 6-8, 11 and 17 under 35 U.S.C. § 103(a) over Kiyama be withdrawn.

B. Rejection of Claims 1, 6-11 and 17 Over Hoffmann

Claims 1, 6-11 and 17 have been rejected as allegedly being obvious over Hoffmann. To the extent that the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

As discussed in section IIB above, amended claims 1, 6-8, 11 and 17 are novel over the compounds of Hoffmann. The compounds of the present invention are ***structurally different*** from those disclosed in Hoffmann and none of the compounds of Hoffmann are embraced in the presently claimed compounds of Formula I of amended claim 1. In addition, there are no teachings or suggestions in Hoffmann to modify the compounds of Hoffmann to

arrive at the compounds of the presently claimed invention. Accordingly, Applicants respectfully request the rejection of claims 1, 6-8, 11 and 17 under 35 U.S.C. § 103(a) over Hoffmann be withdrawn.

C. Rejection of Claims 1, 6, 9, 10 and 17 Over Cuccia

Claims 1, 6, 9, 10 and 17 have been rejected as allegedly being obvious over Cuccia. To the extent that the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

As discussed in section II D above, amended claims 1, 6-8, 11 and 17 are novel over the compounds of Cuccia. The compounds of the present invention are ***structurally different*** from those disclosed in Cuccia and none of the compounds of Cuccia are embraced in the presently claimed compounds of Formula I of amended claim 1. In addition, there are no teachings or suggestions in Cuccia to modify the compounds of Cuccia to arrive at the compounds of the presently claimed invention. Accordingly, Applicants respectfully request the rejection of claims 1, 6, 9, 10 and 17 under 35 U.S.C. § 103(a) over Cuccia be withdrawn.

D. Rejection of Claims 1, 6, 9, 10 and 17 Over Wood

Claims 1, 6, 9, 10 and 17 have been rejected as allegedly being obvious over Wood. To the extent that the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

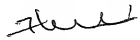
As discussed in section IIE above, amended claims 1, 6-8, 11 and 17 are novel over the compounds of Wood. The compounds of the present invention are ***structurally different*** from those disclosed in Wood and none of the compounds of Wood are embraced in the presently claimed compounds of Formula I of amended claim 1. In addition, there are no teachings or suggestions in Wood to modify the compounds of Wood to arrive at the compounds of the presently claimed invention. Accordingly, Applicants respectfully request the rejection of claims 1, 6, 9, 10 and 17 under 35 U.S.C. § 103(a) over Wood be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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